

REMARKS

Formalities

Claims 25-29 have been allowed. Claims 30-34 were rejected. Claims 1-24 and 31-34 have been canceled. Claim 30 has been amended. The amendments to the claims do not add or constitute new matter. Support for the amendments may be found throughout the specification and originally filed claims. More particularly, support for the amendment to claim 30 may be found, for example, at page 12, line 8 through page 15, line 2 and at page 51, line 24 through page 55 of the specification.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are meant to constitute a proper response to the final rejection. The amendments are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, 25-30 are pending in the instant application.

Rejections

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 30 and 31 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully traverses this rejection.

Specifically, the Examiner asserts that the claims are allegedly incomplete for omitting essential steps, such omission amounting to a gap between the steps. More particularly, the Examiner states that the claims omit the step of “selection of ES cells that undergo homologous recombination.” Further, the Examiner states that recitation of the phrase “wherein the pseudopregnant mouse gives birth” renders the claims indefinite in that a pseudopregnant mouse cannot give birth. The Applicant disagrees with the Examiner’s conclusions, and submits that the method recited in claim 30 is definite and clearly points out the steps necessary for the skilled artisan to utilize the method. However, as the rejection is final, Applicant has overcome the

rejection by canceling claim 31 and amending claim 30 to address each of the Examiner's concerns. Applicant respectfully requests withdrawal of the rejection.

Applicant submits that the pending claims are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 103

Claims 32-34 were rejected as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Mansour *et al.*, 1988, *Nature* 336(24):348-352 ("Mansour"), in view of Guo *et al.*, 2000, *Genomics* 64:241-251 ("Guo"). Applicant respectfully traverses this rejection.

Mansour describes a general approach for isolating embryonic stem cells containing a targeted mutation in a gene, provided that a cloned fragment of the gene is available. Specifically, Mansour teaches the targeted disruption of the *hpri* gene and the proto-oncogene *int-2* in mouse embryo-derived stem cells by homologous recombination using targeting constructs pRV9.1/TK and pINT-2-N/TK, respectively. The Examiner concedes, however, that Mansour does not teach how to make a PKDL2 targeting construct and knockout mouse.

Guo, according to the Examiner, characterizes members of the polycystin family, and describe the cloning of PKLD2 in mouse and human, and allegedly teach that PKDL2 belongs to a subgroup PKD2, the members of which share structural homology with cation channels such as voltage gated cation channel families. Guo further disclose a potential role for PKDL2 in 5q syndrome.

The Examiner has rejected claims 32-34 for the same reasons as applied to the obviousness rejection of claims 1-9 previously. In the previous Office Action (dated June 3, 2003), the Examiner asserted that the ordinary artisan would have been motivated to make a PKDL2 knockout construct for making a transgenic knockout mouse in order to study the precise role PKDL2 plays in facilitating membrane permeability or whether it has any implication in 5q syndrome, as suggested by Guo. The Examiner further asserted that the ordinary artisan would have had a reasonable expectation of success because of the teachings of Mansour and Guo, in light of the high level of skill in the art. The Applicant respectfully disagrees. However, in order to overcome the final rejection, Applicant has canceled claims 32-34.

As the rejection under 35 U.S.C. § 103 is no longer relevant, and pending claims 25-30 are not obvious in view of the sole or combined teachings of Mansour or Guo, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103.

Objections

Claim 31 has been objected to by the Examiner under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 28. Applicants disagree. However, in light of the cancellation of claim 31, Applicant has overcome the objection.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-325.

Respectfully submitted,

Date: March 2, 2004

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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 7590 | | 12/02/2003 | | |
| Deltagen, Inc. 740 Bay Road Redwood City, CA 94063 | | | EXAMINER QIAN, CELINE X | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1636 | |

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FINAL OFFICE ACTION

RESP DUE 3.2.04

| |
|------------------------|
| RECEIVED |
| DEC - 8 2003 |
| BY: <i>[Signature]</i> |

Office Action Summary

Application No.

10/005,211

Applicant(s)

ALLEN, KEITH D.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-13 and 20-34 is/are pending in the application.
- 4a) Of the above claim(s) 10-13 and 20-24 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 25-29 is/are allowed.
- 6) ☒ Claim(s) 30-34 is/are rejected.
- 7) ☒ Claim(s) 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 July 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claims 10-13, 20-34 are pending in the application. Claims 10-13, 20-24 are withdrawn from consideration for being directed to non-elected subject matter. Claims 25-34 are currently under examination.

This Office Action is in response to the Amendment filed on 9/8/03.

Response to Amendment

The rejection of claims 1-9 and 14-19 under 35 U.S.C. 112 1st paragraph is moot in light of Applicant's cancellation of the claims.

The rejection of claims 1, 2, 8, 14 and 15 under 35 U.S.C. 112 2nd paragraph is moot in light of Applicant's cancellation of the claims.

The rejection of claims 1-9 under 35 U.S.C. 103 (a) is moot in light of Applicant's cancellation of the claims.

Claims 30 and 31 are rejected under 35 U.S.C. 112 2nd paragraph for reasons discussed below.

Claims 32-34 are rejected under 35 U.S.C. 103 (a) for reasons set forth of the record mailed on 6/3/03 and further discussed below.

Claim 31 is objected to for reasons discussed below.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: selection of ES cells that undergo homologous recombination.

The recitation of "wherein the pseudopregnant mouse gives birth" renders the claims indefinite because a pseudopregnant mouse cannot give birth. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mansour et al. (1988, Nature, vol. 336, No. 24, 348-352), in view of Guo et al. (AF).

Claims 32-34 are rejected under 35 U.S.C. 103 (a) for same reason as applied to claims 1-9 set forth in the previous office action. The recitation of "wherein the target construct, when introduced into... exhibits anti-depressive behavior when compared to a wild type mouse" is intended use for the claimed targeting construct. Such recitation does not carry patentable weight. Therefore, the rejection still applies to these claims.

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Mansour et al. teach a strategy for targeted disruption of the *hprt* gene and proto-oncogene *int-2* in mouse embryonic stem cells and subsequent generation of knockout mice. Their teaching addresses the previous technical difficulty of obtaining embryonic stem cell carrying non-selectable, targeted gene mutation at loci of interest, and therefore provides a model which can be used to produce homozygous mutation of any gene, regardless of its function, if a cloned fragment of the gene is available (see page 348, second paragraph, line 1-3, third paragraph, line 1-5, and page 352, fourth paragraph, line 1-3). Mansour et al. further teach the generation of two targeting constructs, pRV9.1/TK and pINT-2-N/TK, each contains two sequences from an *hprt* gene and an *int-2* gene respectively, and a neo selection marker gene in between the two sequences (see page 350, figure 3). However, Mansour et al. do not teach how to make a PKDL2 target construct and knockout mouse.

Guo et al. teach that mutations in PKD1, PKD2, PKDL and REJ are four known member of polycystins that share significant homology with each other (see page 241, 1st col. lines 1-4). Guo et al. teach the cloning and characterization of a novel polycystin family member PKDL2 in mouse and human. Guo et al. further provide the nucleic acid sequence encoding Guo et al. teach the cloning and characterization of a novel polycystin family member PKDL2 (see page 243, Figure 1). Guo et al. teach that knockout mouse models of PKD1 and PKD2 illustrate their critical role in the development of kidney and pancreas. Guo et al. also teach that PKDL2 belong to PKD2 subgroup and share structural homology with cation channels such as voltage gated Ca^{+} , Na^{+} and K^{+} channel families. Guo et al. further teach that PKDL2 might be implicated in 5q syndrome.

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It would have been obvious to one of ordinary skill in the art at the time of filing to make a PKDL2 knockout construct to generate a cell deficient of PKDL2 protein or a PKDL2 transgenic knockout mouse because of the combined teachings of Mansour et al. and Guo, which provide a general method of making targeted disruption of specific gene in mouse genome to study its function and the importance in studying the PKDL2 function. The ordinary artisan would have been motivated to do so to study the precise role PKDL2 plays in facilitate membrane permeability or whether it has any implication in 5q syndrome. The level of skill in the art of making gene targeting constructs and subsequently generating knockout mouse is high, absent evidence to the contrary, one of ordinary skill in the art would have reasonable expectation of success to make a PKDL2 knockout construct as claimed. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Objections

Claim 31 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 28. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

Claims 25-29 are allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

This application contains claims 10-13 and 20-24 drawn to an invention nonelected with traverse in the amendment filed on 5/5/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER